

### **REMARKS**

Claims 1, 7, 8, 10, 17-19, 22, 26, 33-39, 44, 50, 54-56, 61-68, 71-73, 77, 78, 83-86, 92-94, 101-103, 106, 110, 117-121, 129, 133, 136, 140-144, 147, 149, 155, 158, 163, 165, 172, 176, 179, 180, 183, 184, 187-189, 195, 196, 202, 206, 208, 214, 216, 219, 221, 223, 225, 228, 247, 252, 255-257, 261, 267, 271-283, 285, 287, 289, 291, 293, 294, 296, 299, 302-304 and 307-315 are hereby canceled. As a result, Claims 231, 316-324 are pending for examination. No new matter has been added. Applicant respectfully requests entry of the amendment.

### **Claim Objections**

The Examiner objected to the claims because applicant did not indicate the status of certain of the claims as withdrawn. Applicant believes the status was indicated correctly at the time, as the Examiner had not yet formally withdrawn the claims from examination. Nonetheless, the withdrawn claims are cancelled by the present amendment and indicated as such in this amendment. It is believed that the objection has been addressed, and it is requested that the objection be withdrawn.

### **Interview Summary**

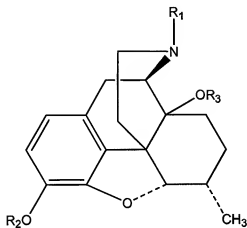
The Examiner is thanked for the courtesy extended during the interview conducted on October 9<sup>th</sup>, 2008, the substance of which is detailed here. Both the claims and the prior art were discussed. Moreover, Applicant explained that the present claims are drafted to protect one of several inventions described in the present application; one that embodies several findings made by Applicant. Among other things, Applicant discovered the problem, unexpected given that methyl naltrexone ("MNTX") had been studied since the late 1970s (see U.S. Patent 4,176,186), that solutions of MNTX are not stable under relevant conditions (e.g., during autoclaving, over extended periods of time, etc). As described in the present application and discussed in the interview, Applicant discovered various ways to solve this problem. One particular approach is recited in the present claims. That approach involves a MNTX solution with *both* (1) a chelating agent, and (2) a pH from 2 to 6. As discussed in the interview and set forth in the specification, Applicant

discovered surprising and unexpected beneficial effects (synergies) of combining these two features. For example, among other things, Applicant found that, when a chelating agent is used, a MNTX solution can be prepared that is stable at a broader range of pHs.

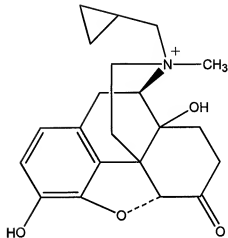
In the Interview Summary Report, the Examiner characterized Applicant's points as asserting "the *criticality* of the claimed pH and chelating agent combined in the solution of methylnaltrexone". Applicant wishes to clarify that Applicant has not asserted that the combination of pH and chelating agent as recited in the present claims is *critical* to providing a stable MNTX solution, as either one alone can provide a MNTX solution with improved stability. However, the present claims are directed only to those embodiments of the present invention that include both elements, and Applicant has demonstrated particularly unexpected and beneficial aspects of the claimed combination.

#### **Outstanding Rejection Under 35 U.S.C. § 103**

The Office Action included a rejection of the pending claims as obvious over US Patent No. 4,322,426 to Hermann ("Hermann") in view of Remington's. The rejection states that Hermann describes a pharmaceutical formulation of MNTX (though, as acknowledged, does not recite the claimed chelating agent or pH). In fact, however, as discussed in the interview, Hermann *does not* describe MNTX but instead describes *different* compounds. For example, Hermann relates to tertiary amines; methylnaltrexone is a quaternary amine.



Hermann et al. US Patent No. 4,322,426



Methylnaltrexone

Thus, as discussed at the interview, the levied rejection should be removed.

Applicant respectfully submits that, for all of the reasons set forth above and discussed at the interview, the pending claims are in condition for allowance. A notice to that effect is respectfully requested.

Dated: 11/17/08

Respectfully submitted,

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